

PATENT
10/039,956
Docket 091/009c

CLAIM AMENDMENTS

1. *(Withdrawn)* A composition comprising proliferating primate pluripotent stem (pPS) cells, which is essentially free of feeder cells.

2 to 15. *CANCELLED*

16. *(Currently amended)*

A method of screening a substance, comprising:

~~contacting a differentiated cell with the substance, and, determining any phenotypic or metabolic changes in the cell that result from contact with the compound, and correlating the change with cellular toxicity or modulation; wherein the differentiated cell has been obtained by:~~

~~a) obtaining a line of human embryonic stem cells growing on an extracellular matrix instead of feeder cells; and~~

~~b) causing cells in the culture to differentiate into the population of differentiated cells~~

a) contacting a population of differentiated cells with the substance;

b) determining any phenotypic or metabolic change in the cell that results from contact with the substance, and

c) correlating the change with cellular toxicity or modulation;

wherein the differentiated cells are obtainable by growing human embryonic stem (hES) cells on an extracellular matrix instead of feeder cells, but in a medium conditioned by feeder cells, and then causing or permitting the hES cells to differentiate.

17 to 36. *CANCELLED*

37. *(Currently amended)* A method of screening a substance, comprising:

a) obtaining a culture of undifferentiated pPS cells proliferating on an extracellular matrix instead of feeder cells but in a medium conditioned by feeder cells;

b) optionally causing or permitting the pPS cells to differentiate; then

c) combining the cells with the substance; and

d) determining any effect of the substance on the cells.

38. *(Previously presented)* The method of claim 37, wherein the extracellular matrix upon which the undifferentiated pPS cells are cultured is Matrigel® basement membrane matrix, laminin, or collagen.

PATENT
10/039,956
Docket 091/009c

39. *(Previously presented)* The method of claim 37, wherein the cells are undifferentiated when contacted with the substance.
40. *(Previously presented)* The method of claim 37, wherein the cells have been caused or permitted to differentiate before being contacted with the substance.
41. *(Previously presented)* The method of claim 40, wherein the cells have been caused to differentiate by a process comprising replating them onto a surface that promotes differentiation.
42. *(Previously presented)* The method of claim 40, wherein the cells have been caused to differentiate by adding component(s) to the medium that promote differentiation towards a particular cell lineage.
43. *(Previously presented)* The method of claim 40, comprising causing the cells to differentiate into cells having characteristics of neuronal cells, glial cells, or neural precursors.
44. *(Previously presented)* The method of claim 40, comprising causing the cells to differentiate into cells having characteristics of hepatocytes.
45. *(Previously presented)* The method of claim 37, wherein the pPS cells are human embryonic stem (hES) cells.
46. *(Previously presented)* The method of claim 37, comprising determining the effect of the substance on growth of the cells.
47. *(Currently amended)* The method of claim 37, comprising determining whether the compound substance affects differentiation of the cells.
48. *(Currently amended)* The method of claim 37, comprising determining whether the compound substance affects expression of a marker or receptor by the cells.
49. *(Currently amended)* The method of claim 37, comprising determining whether the compound substance affects release of a marker or enzyme from the cells.
50. *(Currently amended)* The method of claim 37, comprising determining whether the compound substance affects DNA synthesis or repair in the cells.

PATENT
10/039,956
Docket 091/009c

51. *(Previously presented)* The method of claim 37, comprising analyzing the cells by metaphase spread.
52. *(Previously presented)* The method of claim 37, comprising determining whether the ~~compound~~ substance is toxic to the cells.
53. *(Currently amended)* A method of screening a substance for its effect on undifferentiated human embryonic stem (hES) cells, comprising:
a) obtaining a culture of undifferentiated pPS cells proliferating on an extracellular matrix instead of feeder cells , but in a medium conditioned by feeder cells;
b) combining the undifferentiated hES cells with the substance; and
c) determining any effect of the substance on the cells.
54. *(Previously presented)* The method of claim 53, comprising determining the effect of the substance on growth of the cells.
55. *(Currently amended)* The method of claim 53, comprising determining whether the ~~compound~~ substance affects differentiation of the cells.
56. *(Currently amended)* The method of claim 53, comprising determining whether the ~~compound~~ substance affects expression of a marker or receptor by the cells.
57. *(Currently amended)* The method of claim 53, comprising determining whether the ~~compound~~ substance is toxic to the cells.
58. *(Previously presented)* The method of claim 16, comprising causing the cells to differentiate into cells having characteristics of neuronal cells, glial cells, or neural precursors.
59. *(Previously presented)* The method of claim 16, comprising causing the cells to differentiate into cells having characteristics of hepatocytes.
60. *(Previously presented)* The method of claim 16, comprising determining the effect of the substance on growth of the cells.
61. *(Previously presented)* The method of claim 16, comprising determining whether the compound affects expression of a marker or receptor by the cells.

PATENT
10/039,956
Docket 091/009c

62. *(Previously presented)* The method of claim 16, comprising determining whether the compound is toxic to the cells.
63. *(New)* The method of claim 37, wherein the feeder cells used to condition the medium are fibroblasts.
64. *(New)* The method of claim 37, wherein the feeder cells used to condition the medium are mesenchymal cells.
65. *(New)* The method of claim 37, wherein the feeder cells used to condition the medium were obtained by differentiating pPS cells.
66. *(New)* A method of screening a substance for its effect on undifferentiated hES cells, comprising:
 a) combining the substance with a population of undifferentiated hES cells that is free of feeder cells; and
 b) determining any effect of the substance on the cells.
67. *(New)* The method of claim 66, comprising determining whether the substance affects differentiation of the cells.

PATENT
10/039,956
Docket 091/009c

68. (New) The method of claim 66, comprising determining whether the substance affects expression of a marker or receptor by the cells.

69. (New) The method of claim 66, comprising determining whether the substance is toxic to the cells.

Upon allowance of the application, please renumber the claims as follows:

Claim	1	→	35
	16	→	29
	37	→	1
	38	→	2
	39	→	6
	40	→	7
	41	→	8
	42	→	9
	43	→	10
	44	→	11
	45	→	12
	46	→	13
	47	→	14
	48	→	15
	49	→	16
	50	→	17
	51	→	18
	52	→	19
	53	→	20
	54	→	21

Claim	55	→	22
	56	→	23
	57	→	24
	58	→	30
	59	→	31
	60	→	32
	61	→	33
	62	→	34
	63	→	3
	64	→	4
	65	→	5
	66	→	25
	67	→	26
	68	→	27
	69	→	28